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3D Modelling of droplet formation in two-phase microfluidics for single-cell manipulation

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Summary:
In this study, the evolving hydrodynamic phenomena were modelled and characterized in complex two-phase micro-fluidic systems, aiming to enhance their applicability in advanced droplet-based single-cell sorting and analytical methodologies. An innovative Computational Fluid Dynamics (CFD) driven multi-dimensional optimization strategy was introduced and applied to explore the influence of geometric configurations and flow parameters. The droplet generation process has been studied by finite element modelling (FEM), utilizing the Laminar Flow and Level Set modules within COMSOL Multiphysics for numerical simulations. The proposed microfluidic system was manufactured and its behaviour was compared to the simulated characteristics. The experimental results supported the comprehension of the droplet formation in case variable volumetric flow rates and the interaction between flow dynamics and channel geometry. The effective control of the resultant droplet size distribution enables to determine the numbers of particles and cells confined.

Keywords: finite element modelling (FEM), two-phase microfluidics, single-cell, droplet formation, LoC

Motivation and Objectives

In the past twenty years, the adoption of micro-engineered systems has transformed the high-throughput analysis methods applied in the fields of chemical and biological sciences. Droplet-based microfluidic systems generate and manipulate distinct, physically separated fluid volumes or droplets. These multi-phase flow systems enable to utilise a wide range of easily accessible techniques for manipulating droplets, including splitting, merging, mixing, dilution and incubation. Droplets produced within two-phase microfluidic setups serve as optimal vessels for high-throughput cell screening applications. The response of individual cells to physical and chemical effects can be precisely examined in the micro-environment at the scale of cell size. This study employs high-performance finite element modelling (FEM) of these multi-phase systems for a thorough examination of hydrodynamic droplet generation process, primarily focusing on the effects of different flow rates and geometric parameters [1].

Fluid Dynamic Simulation Methods

COMSOL Multiphysics simulation code was employed to examine the droplet formation process in 3D two-phase models, aiming for a more precise understanding of the evolving flow characteristics. The analysis relies on numerically solving the governing Navier-Stokes and continuity equations. To characterize and compare microfluidic systems, the Capillary number (Ca) served as a commonly utilized parameter. Regarding droplet generation, including evolving droplet diameters and generation frequencies, the effects of volume flow ratios at the inlets, fluid viscosity, and interface tension were explored through successive parametric sweep simulations. Details of the main material properties of the fluids are provided in Table 1.

Tab. 1: Main material parameters of fluids

Material	Dynamic viscosity (μ)	Density (ρ)
Water	$1.95 \cdot 10^{-3}$ *Pa·s*	10^3 *kg/m*^{3}
Silicon Oil	$20 \cdot 10^{-3}$ *Pa·s*	10^3 *kg/m*^{3}

To manage reliable simulation of multiphase fluid flow, the Level Set technique, a robust computational approach was employed [2, 3]. This method was integrated with the Laminar Flow module to obtain precise results within the microfluidic approaches characterized by a predomi-

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nance of low Reynolds numbers. The droplet diameters were calculated using a self-developed MATLAB script, which based on image analysis.

Numerical Results

According to the simulations, a significant change can be detected in the droplet diameters as the function of the flow rate and different geometric properties (Fig. 1). The average diameter was decreased from 98.27 µm to 62.16 µm when the flow rate of oil increased from 1.2 µl/s to 3.2 µl/s. The flow rate of water remained constant (0.2 µl/s). The size distribution of generated droplets was visualised by histograms created using the MATLAB software (Fig. 2).

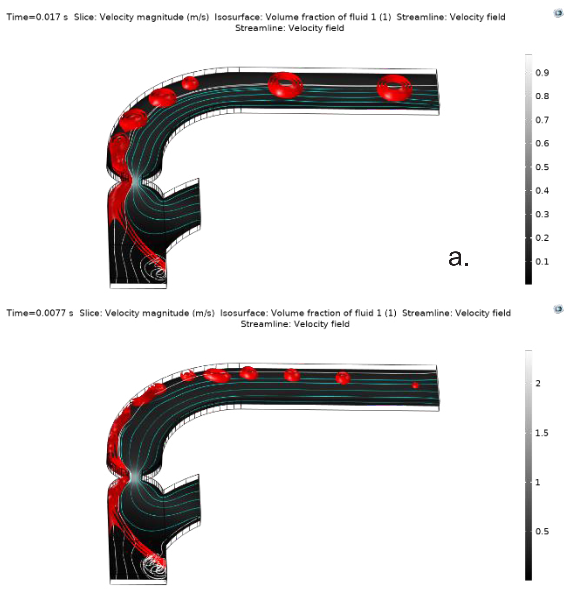

Fig. 1. Droplet generation in the 3D FEM model in the case of two different flow rates. The applied flow rates were: 0.2 µl/s (water), 1.2 µl/s (oil) in Figure 1.a and 0.2 µl/s (water), 3.2 µl/s (oil) in Figure 1.b.

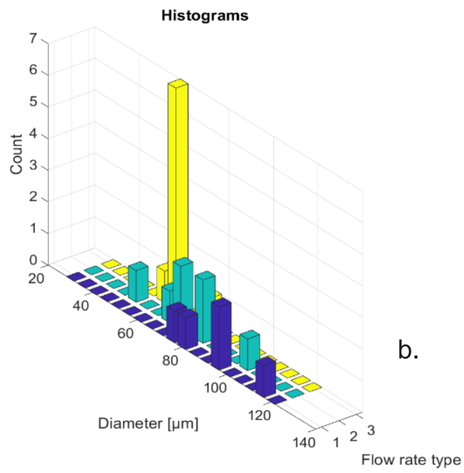

Fig. 2. Droplet size distributions based on the image analysis of the simulated droplet generation. While the flow rate of water was set to a constant value of 0.2 µl/s, three different oil flow rates were varied between 1.2 µl/s (1), 2 µl/s (2), and 3.2 µl/s (3).

Experimental Validation

To validate the numerical model, microfluidic devices were manufactured using soft lithography techniques in Polydimethylsiloxane (PDMS) polymer, featuring various geometrical configurations for droplet generation (Fig. 3). Experimental results indicate that factors such as the wetting characteristics of the aqueous phase significantly affect the frequency of droplet formation, whereas the velocity of the oil phase impacts the droplet size. Elevating either the flow rate of the oil phase or the Capillary number leads to a momentous reduction in droplet diameter.

The obtained results can support the establishment and optimisation of multi-phase microfluidic systems to achieve proposed size of microdroplets applicable as miniaturized reactors or cell containers in Lab-on-a-Chip and Organ-on-chip applications.

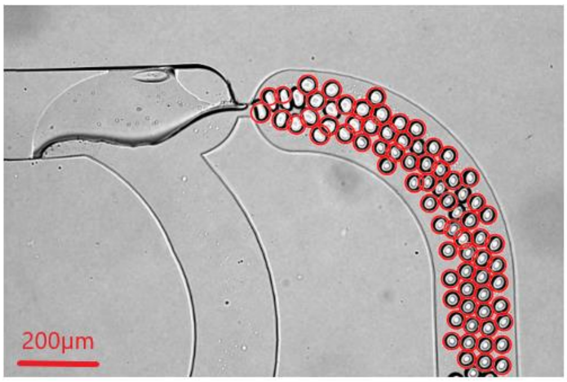

Fig. 3. Laboratory experiment to support the validation simulation results. The flow rate was set as 0.1 µl/s (water), 0.2 µl/s (oil). The droplet diameters were determined by MATLAB. The average diameter was 44.57 µm in this case.

References

[1] K. J. Donovan. „Computational fluid dynamics modeling of two - dimensional and three – dimesional segmented flow in microfluidic chips", San Jose State University, (2014). doi:10.31979/etd.3tzd-y6xm.

[2] H. A. Akhlaghi Amiri, A. A. Hamouda, „Evaluation of level set and phase field methods in modeling two phase flow with viscosity contrast through dual-permeability porous medium", Elsevier, International Journal of Multiphase Flow, (2013)

[3] „Two Methods for Modeling Free Surfaces in COMSOL Multiphysics", url: https://www.comsol.com/blogs/two-methods-for-modeling-free-surfaces-in-comsol-multiphysics/ (last access: 04-24-2024)